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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/117,071	09/25/98	KINGSMAN	A 9192.5US01

HM22/0119

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EXAMINER	
SORBELLO,F	
ART UNIT	**PAPER NUMBER**
1633	18

DATE MAILED: 01/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1- File Copy

PTO-90C (Rev 2/95)

Office Action Summary	Application No.	Applicant(s)
	09/117,071	KINGSMAN ET AL
	Examiner	Art Unit
	Eleanor Sorbello	1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2000 and 26 October 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-56,58-61 and 63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-56,58-61 and 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
18)☐ Interview Summary (PTO-413) Paper No(s).
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other

Response to amendment

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Eleanor Sorbello, Art Unit 1633.

2. Applicant's (1) amendment and response and (2) supplemental amendment and response to the official Office Action mailed March 28, 2000 as Paper No. 13, has been received and filed on October ~~16~~ 3, 2000 as Paper No. 16C, and October 26, 2000 as Paper No. 17 respectively. Claims 47, 51, 59 and 61 have been amended, claims 22-25, 31-34, 41-46, 57, 62 have been canceled, and claims 63 has been added. Claims 47-56, 58-61 and 63 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's argument.

2. Applicant's arguments are addressed below on a per section basis. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 47-56, 58-61 and 63 stand rejected under 35 USC § 112, first paragraph for reasons of record. Applicant's arguments have been fully considered but they are not persuasive. The amended claims are directed to (a) a method for introducing a heterologous gene into a target cell in a subject via a replication defective retroviral vector (b) a producer cell comprising a heterologous gene (c) a method of making a

producer cell *in vivo* in a subject, (d) method of making a replication defective retroviral vector in a subject, and are therefore drawn to the *in vivo or ex vivo* delivery of DNA or nucleotides or genes into a subject, which still falls in the realm of gene therapy. The scope of the amended or newly added claims are not changed necessarily. Applicant's arguments have been fully considered but they are not persuasive.

As stated in the FOAM, the state of the art in gene therapy is such that details and specifics are required to be explicitly stated in order for the specification to be enabled. For instance, for the administration of the retroviral vector to the subject, details regarding the construction, composition, concentration, quantities in which the retroviral vector and site of administration is required to be provided for the each disease to be treated in order for one of skill in the art to be able to make and use the invention without undue experimentation. It is not clear that applicants extrapolation of results from an *in vitro* example using a reporter gene in a retroviral construct in HeLa cells to that which occurs *in vivo* is appropriate due to the factors stated in FOAM and stated herein. In the instant application, applicant's also attempt to extrapolate the results from the example wherein introduction of a reporter gene, LacZ in a construct to the brains, liver and colon of a mouse to that which will occur when a transgene introduced via a defective retroviral vector into a patient suffering from a diseased condition, prophetically resulting in amelioration of the diseased condition. Applicants additionally claim introduction of gene into any cell *in vivo* via a retrovirus thereby converting it into a producer cell for any use in medicine.

Applicants argue that one of skill in the art is familiar with methods of gene delivery into various cell types and that that the onus is not on the applicant to provide examples of each and every delivery method claimed. Applicant additionally states that one of skill in the art could readily devise a suitable method for introducing a DNA sequence encoding a retroviral genome and the packaging components env and gag-pol into a cell. However, the current state of the art as stated in the review articles provided in the FOAM and listed in Form 892, is not so defined that one of skill in the art would anticipate results drawn from *in vitro* results without actually been shown that the results in an analagous *in vivo* example have actually worked. Therefore contrary to applicants argument, the onus is on the applicant to indicate analagous examples that have proven results. This is made clear by the MPEP 608.01(p) where it states: "If the use disclosed is of such nature that the art is unaware of successful treatments with chemically analogous compounds, a more complete statement of how to use must be supplied...".

Applicants also argue that the present system known as vector production system (VPS) used to create an in situ retroviral factory (ISRF), which is a producer cell created from the individuals own cells is known in the art to be different from that stated in the FOAM. Applicants argue that this system is an advance over the previous known systems as it can generate the retroviruses continuously for long periods of time, even years, *in situ*. However, as stated above, applicants have not introduced a therapeutic gene into a cell ex-vivo(from an individual) via a retrovirus resulting in the continuous production of retroviral particles, except by prophetic consideratio

Therefore, due to the state of the art, the nature of the invention, the breadth of the claims the lack of guidance, and unpredictability in the art, one or skill in the art will require undue experimentation to make and use the invention as claimed by applicant.

4. Claims 60, 61 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 60 and 61 are rejected for depending from a cancelled claim.

Claim 63 recites the term "fresh". It is unclear what is meant by this term unless it is specifically defined in the specification.

5. Claims 51 and 59 are rejected under 35 U.S.C. 102 (a) as being anticipated by Garver et al., and are rejected for the same reasons of record.

Claims 51 and 59 are directed to the same elements as were in cancelled claim 31-34. Claims 51 and 59 drawn to a producer cell and method of producing a producer cell that produces replication deficient retroviral vectors comprising (a) first DNA sequence encoding a functional env gene (b) a heterologous DNA sequence and (c) another DNA sequence encoding the functional gag-pol genes. Applicants argue that Garver et al. do not use a second complementing nucleic acid sequence, i.e. one carrying the env gene and another carrying the gag-pol genes. However, to the contrary, Garver et al. (see abstract), states that the producer cell is produced by the simultaneous delivery of two nucleic acid sequences. The first being a replicatior

deficient viral genome, and the second being a nucleic acid that complements the viral sequences deleted from the first nucleic acid.

Conclusion

6. Claims 47-56, 58-61 and 63 are rejected.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication should be directed to Eleanor Sorbello, who can be reached at (703)-308-6043. The examiner can normally be reached on Mondays-Fridays from 6.30 a.m. to 3.00 p.m. EST.

Questions of formal matters can be directed to the patent analyst,

Tracey Johnson, whose telephone number is (703) 305-2982

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Deborah Clark

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